

US EPA ARCHIVE DOCUMENT

Regional Cardiac Blood Flow with Air Particle Exposure

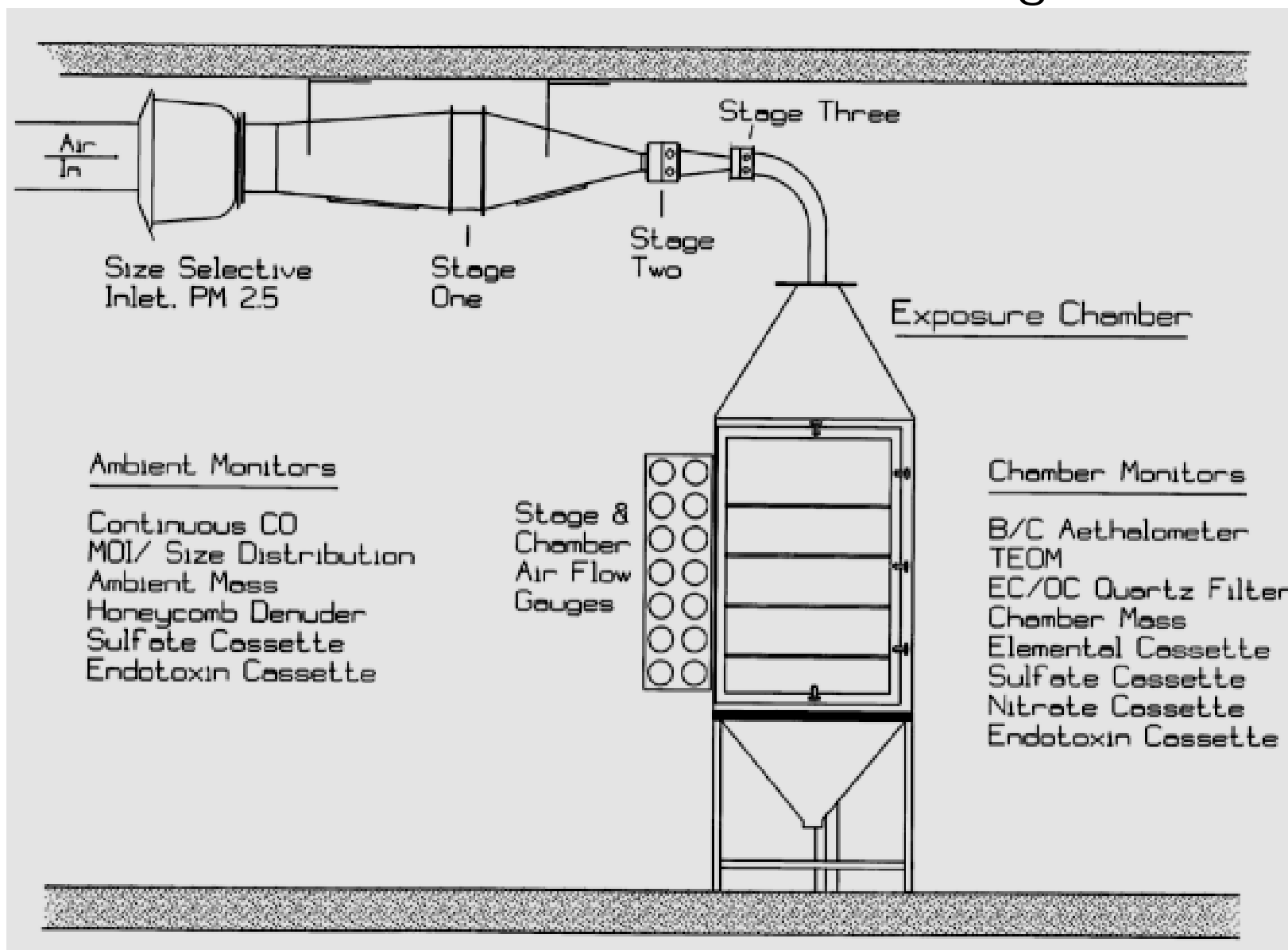
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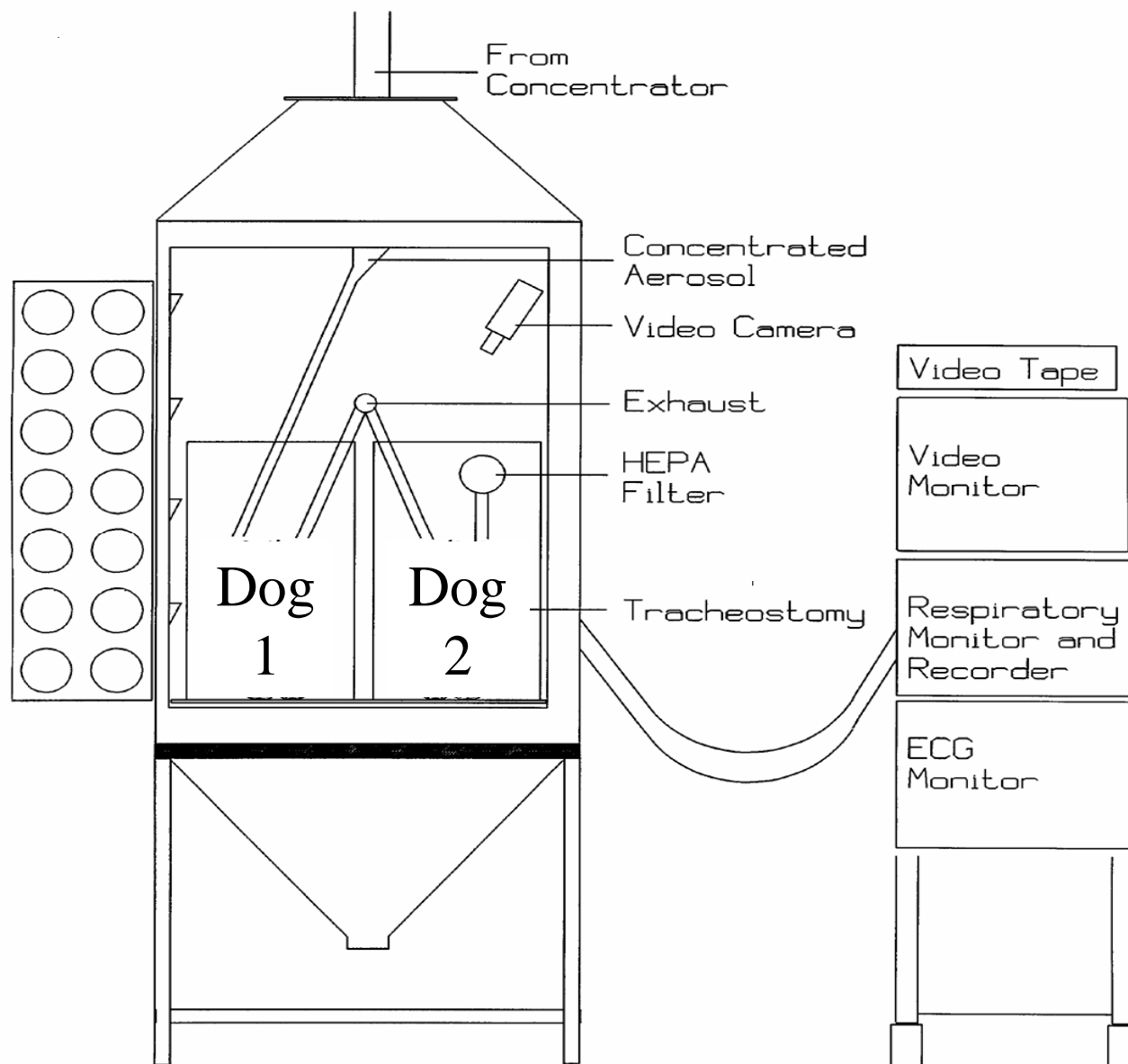
Specific Aims

- To assess mechanisms by which exposure to ambient particles exacerbate myocardial ischemia during acute coronary occlusion through assessment of regional myocardial blood flow.
- To evaluate the role of the autonomic nervous system in regulation of regional myocardial blood flow with coronary occlusion and exposure to ambient particles.

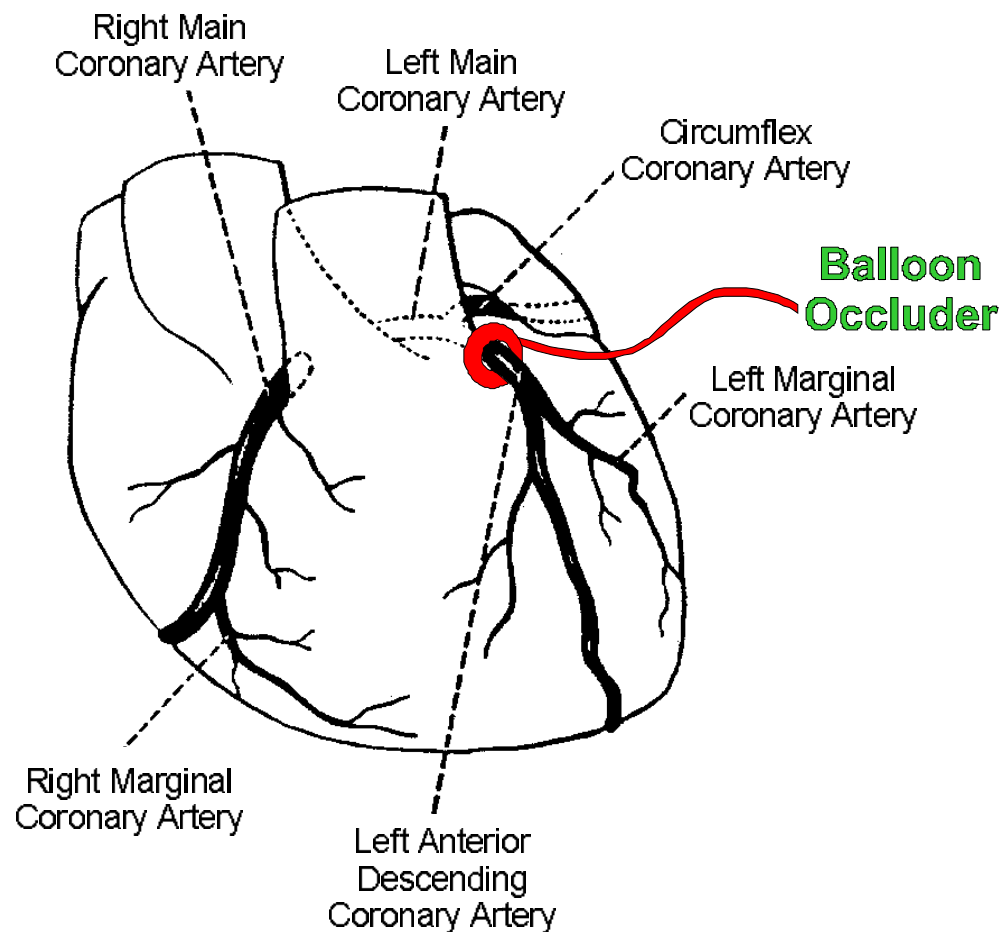
Harvard Ambient Particle Concentrator, Inhalation Chamber and Monitoring Methods



Inhalation chamber setup and physiologic monitors



Canine Myocardial Ischemia Model



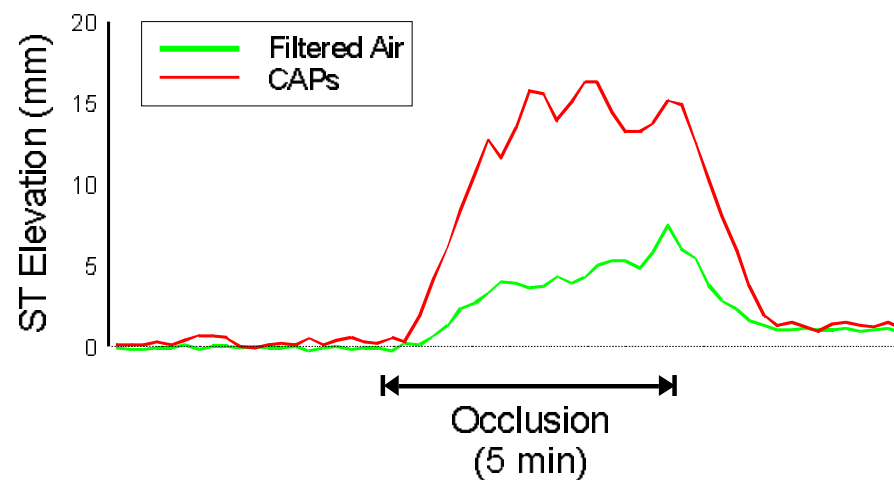
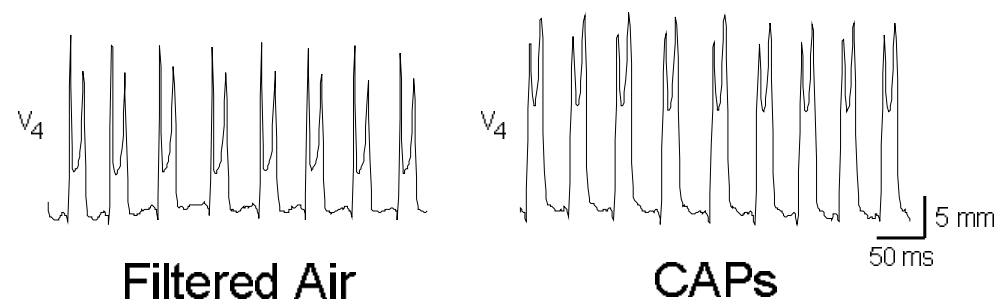
- Implantation of a balloon occluder for coronary artery occlusion
- Two - 5 min occlusions after each CAPs or sham exposure

Exposure Protocol

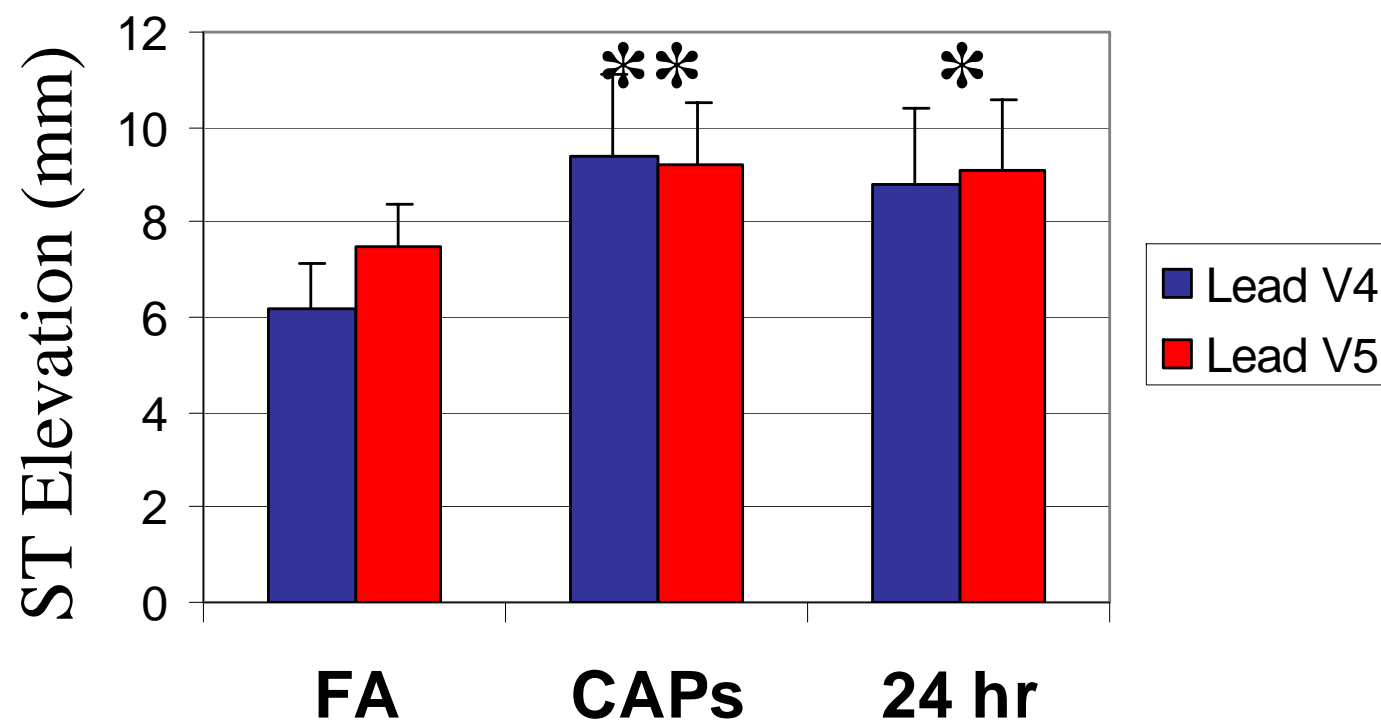
Day	Dog 1	Dog 2
1	Filtered Air	Filtered Air
2	CAPs	Filtered Air
3	Filtered Air	CAPs
4	Filtered Air	Filtered Air

CAPs = Concentrated Air Particles

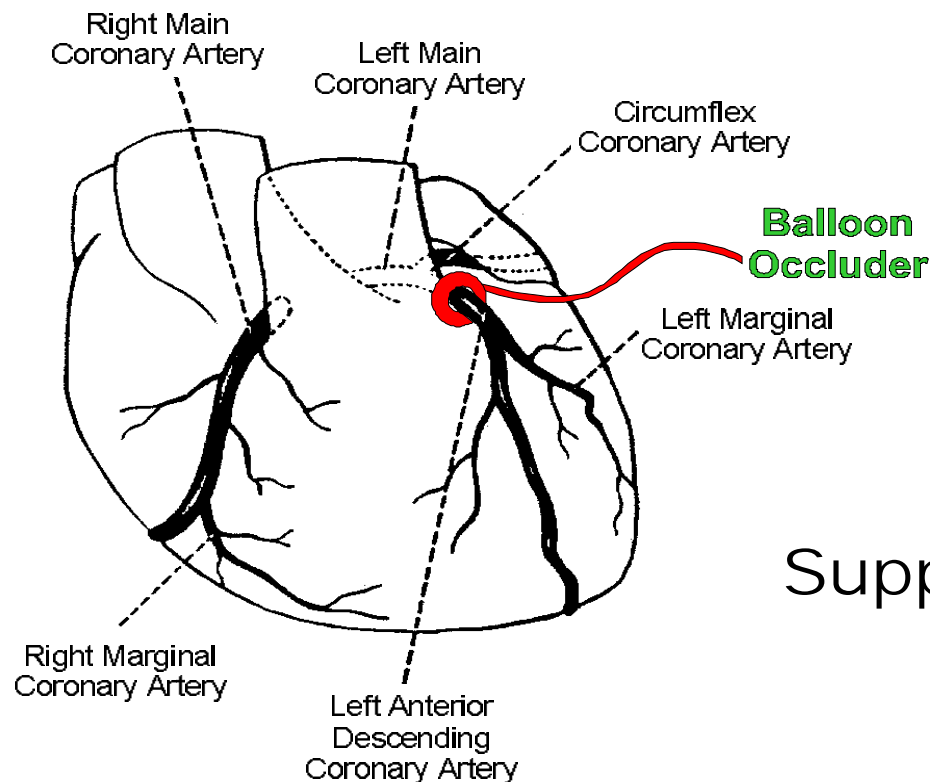
Myocardial Ischemia is Enhanced by CAPs



Peak ST-Segment Elevation



Canine Myocardial Ischemia Model



Supply: myocardial
blood flow

VS

Demand: myocardial
work
 $HR \times BP$

To assess mechanisms by which exposure to ambient particles exacerbate myocardial ischemia during acute coronary occlusion through assessment of regional myocardial blood flow.

Hypothesis: CAPs exposure results in coronary vasoconstriction and decreased collateral blood flow to the area of ischemia.

Model: Dogs with coronary occlusion

Treatments: CAPs
Filtered Air -- Sham

Outcomes: Changes in cardiac blood flow using fluorescent microspheres assessing areas of ischemia, adjacent areas, and remote areas
Preexposure normal flow, Flow during occlusion, and Post exposure flow
ECG and blood pressure by telemetry

Statistics: Comparisons of anatomic areas
- size of ischemic area
- flow to ischemic area

Comparisons of Heart rate, BP, and Myocardial work

Fluorescent Microspheres for Regional Blood Flow Measurement

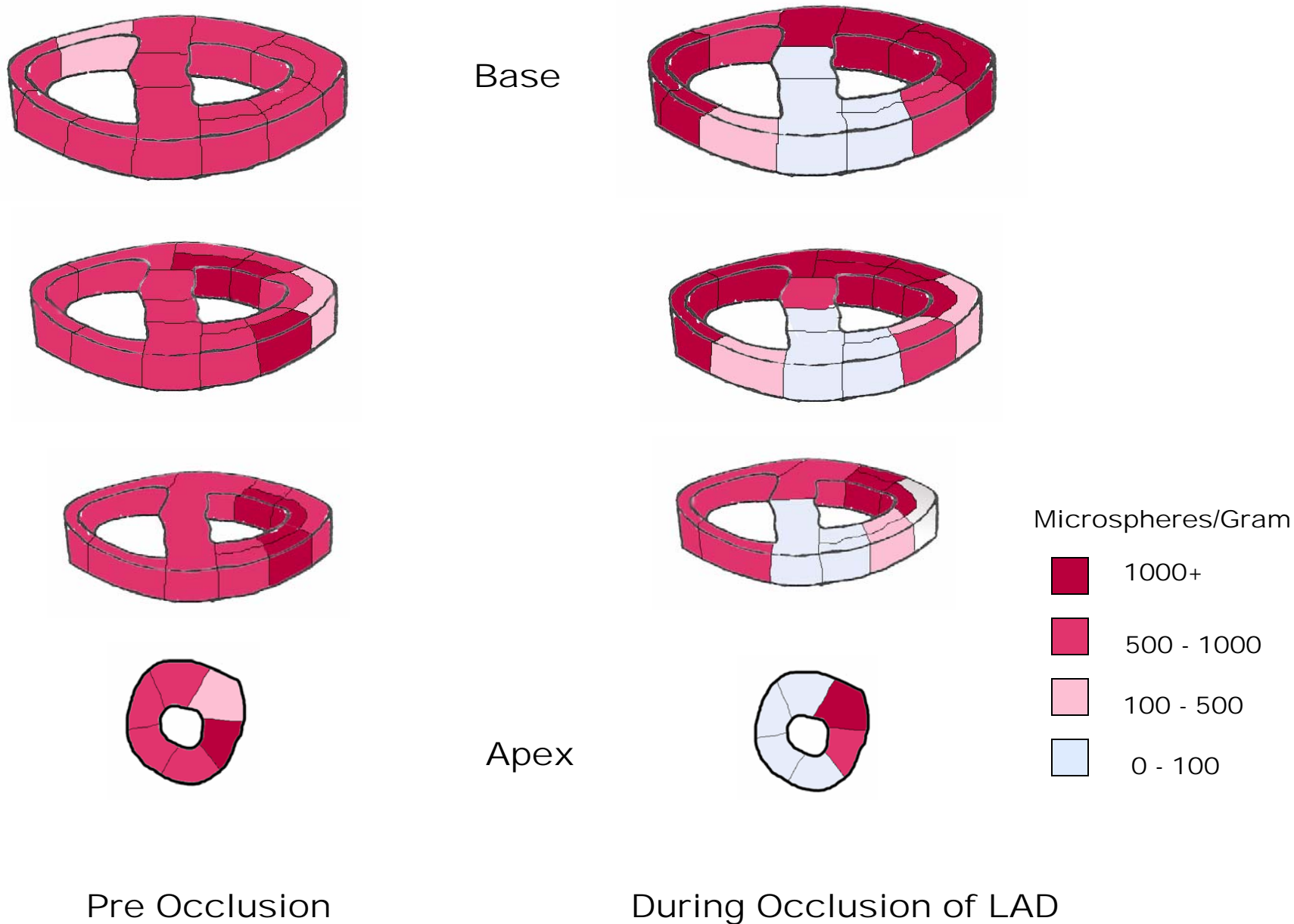
- 15 μm spheres
- 8 colors
- 400 microspheres per tissue piece
 - $N_{\text{min}} - 400(n) [Q_{\text{organ}}/Q_{\text{total}}]$
 - N_{min} – minimum number needed for injection
 - N – total number of organ pieces
 - $[Q_{\text{organ}} / Q_{\text{total}}]$ = fraction of total cardiac output supplying the organ
- Recovery from tissue pieces and blood samples
 - Potassium hydroxide tissue digestion
- Filtration
- Extraction of dyes
- Read in spectrofluorometer
- Calculate flow to each piece in ml/gm/min

Different Colors Permit Multiple Measures In the same Animal

Color	Excitation (nm)	Emission (nm)
Blue	360	423
Blue-Green	420	467
Green	450	488
Yellow-Green	495	506
Orange	534	552
Red	566	598
Crimson	610	635
Scarlet	646	680

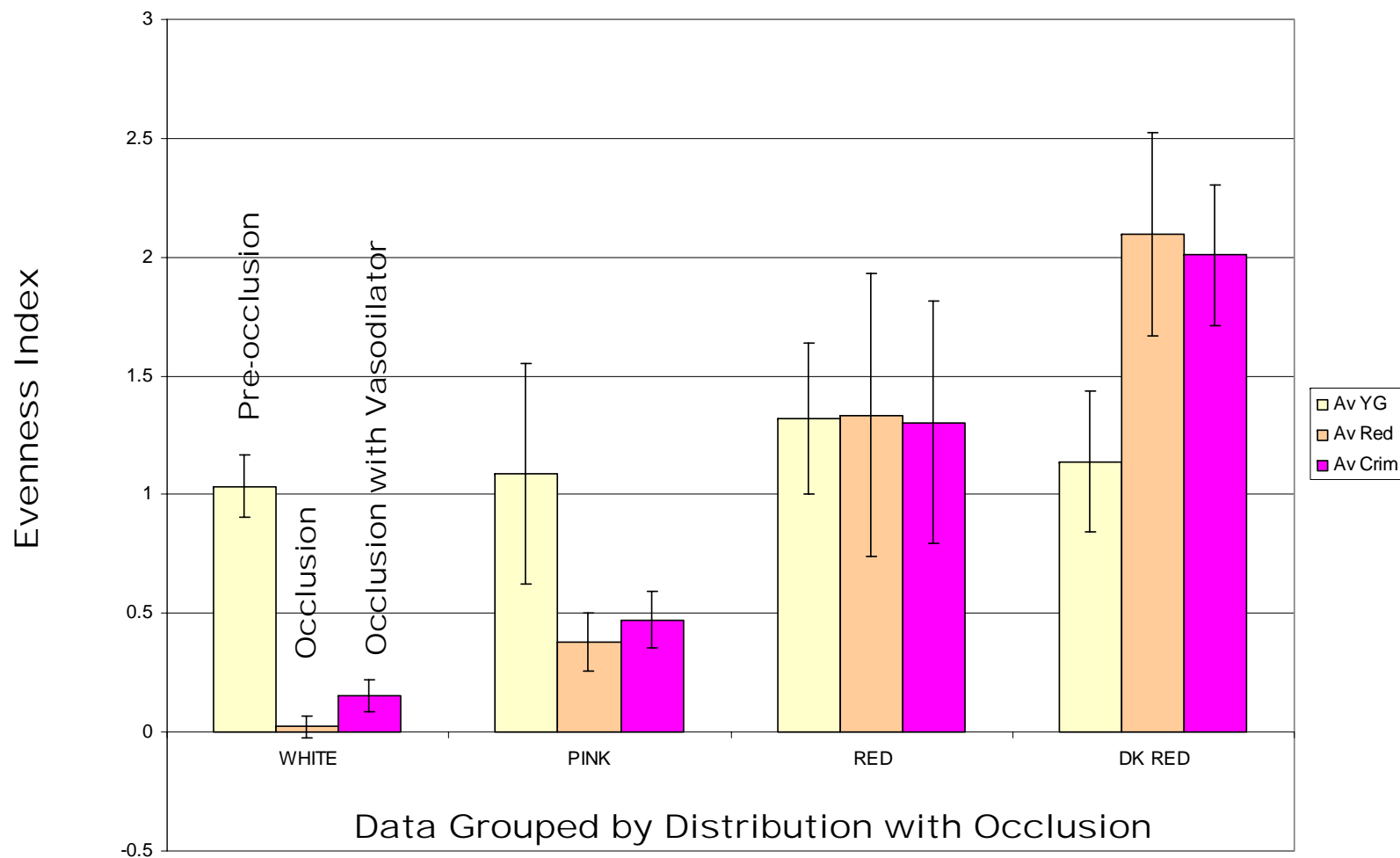
Optimal Excitation and Emission Wavelengths of
FluoSpheres® in 2-ethoxyethyl acetate

Coronary Artery Flow Patterns with Microspheres



Quantification of Cardiac Blood Flow Pre-occlusion, Occlusion and Occlusion with Vasodilator

Evenness Index: $\frac{\text{Microspheres/piece}}{\text{Total Microspheres/Heart}}$



To evaluate the role of the autonomic nervous system in regulation of regional myocardial blood flow with coronary occlusion and exposure to ambient particles.

Hypothesis: CAPs exposure results in coronary vasoconstriction via the sympathetic nervous system resulting in decreased collateral blood flow to the area of ischemia.

Models: Dogs with coronary occlusion, Stellectomy, parasympathetic antagonists

Treatments: CAPs vs Filtered Air -- Sham

Outcomes: Changes in cardiac blood flow using fluorescent microspheres assessing areas of ischemia, adjacent areas, and remote areas

Preexposure normal flow, Flow during occlusion, and Post exposure flow

ECG and blood pressure by telemetry

Statistics: Comparisons of anatomic areas

- size of ischemic area

- flow to ischemic area

Comparisons of Heart rate, BP, and Myocardial work